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(54) IMPROVEMENTS IN AND RELATING TO INGESTIBLE, TOPICAL AND OTHER COMPOSITIONS CONTAINING PHYSIOLOGICAL COOLING AGENTS

(71) We, WILKINSON SWORD LIMITED, a British Company, of Sword Works, Southfield Road, London W.4., do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to ingestible, topical and other compositions having a physiological cooling effect on the skin and on the mucous membranes of the body, particularly the mucous membranes of the nose and bronchial tract.

Menthol is well known for its physiological cooling effect on the skin and mucous membranes of the mouth and has been extensively used as a flavouring agent (menthol being a major constituent of oil of peppermint) in foodstuffs, beverages, dentifrices, mouthwashes, etc. and as a component in a wide range of toiletries, liniments and lotions for topical application. Menthol is also a well known tobacco additive for producing a "cool" sensation in the mouth when smoking.

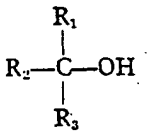
It is well established that the "cooling" effect of menthol is a physiological effect due to the direct action of menthol on the nerve endings of the human body responsible for the detection of hot or cold and is not due to latent heat of evaporation. It is believed that the menthol acts as a direct stimulus on the cold receptors at the nerve endings which in turn stimulate the central nervous system.

Although menthol is well established as a physiological coolant its use, in some compositions, is circumscribed by its strong minty odour.

Certain acyclic alcohols having a structure related to menthol, e.g. 2,4,6 - trimethyl - 4 - heptanol have also been reported as having a physiological cooling effect coupled with a minty odour similar to that of menthol, see Parfums-Cosmetiques-Savons, May 1956, pages 17—20.

The present invention is based on the discovery that certain other acyclic alcohols, which can be readily synthesised, have a physiological cooling effect similar to that obtained with menthol, but do not have the strong odour characteristic of menthol. Indeed in many cases the compounds have a pleasant fruity odour. Such compounds therefore find utility as flavouring or perfuming agents in a wide range of ingestible and topical compositions. More particularly they find utility as components in compositions for nasal application and in vapour rubs and liniments.

The compounds having a physiological cooling effect and utilised in accordance with the present invention are secondary and tertiary alkanols of the formula



where R_1 is H or C_1—C_5 alkyl; R_2 is C_2—C_5 alkyl; R_3 is C_2—C_5 alkyl; with the provisos that, i) when R_1 is H, at least one of R_2 and R_3 is a branched chain group; ii) when R_1 is methyl and one of R_2 and R_3 is isobutyl, the other is selected from ethyl, *n* - propyl, isopropyl, *n* - butyl, sec.butyl, tert.butyl and straight and branched chain amyl; and iii) R_1, R_2 and R_3 together provide a total of from 7—10 carbon atoms.

In accordance with the present invention, we provide a manufactured product for application to or consumption by the human body comprising a physiologically active ingredient capable of stimulating the cold receptors of the nervous system of the body and a carrier therefor, said carrier constituting or providing a vehicle by means of which said ingredient may be brought into contact with the skin or other surface tissue of the body upon use of the said product, said carrier comprising a manufactured article or preparation into which the said ingredient is incorporated by admixture or impregnation and being other than a liquid or mixture of liquids which serve as solvent for the said ingredient and which contain no other ingredient, said physiologically active ingredient being a secondary or tertiary alkanol of the formula given above.

The invention also extends to a method of stimulating the cold receptors of the nervous system of the body, other than as part of a medical treatment, which comprises applying to the skin, or other surface tissues of the body, a compound of the formula defined above.

The most preferred compounds used in the present invention are secondary alkanols of the above formula, i.e. where R_1 is H, containing from 7—9 carbon atoms contributed by R_2 and R_3 together, and at least one of R_2 and R_3 having branching in an alpha or beta position relative to the C atom shown in the formula, and tertiary alkanols of the above formula where R_1 is methyl, ethyl or propyl, and R_1, R_2 and R_3 together contributing from 8—10 carbon atoms, and most preferably at least one of R_2 and R_3 having branching in an alpha or beta position.

Typical alkanols falling within the above formula and utilisable in the compositions of the present invention are indicated in the following Table together with an indication of their relative activities as a stimulant for the cold receptors of the nervous system of the human body. The greater number of stars, the greater the activity, i.e. the greater the cooling effect produced by a given quantity of the compound.

TABLE

R_1	R_2	R_3	Activity	Odour
n-C_3H_7	n-C_3H_7	iso-C_3H_7	*****	woody-caphoraceous
n-C_3H_7	iso-C_3H_7	iso-C_3H_7	*****	camphor-eucalyptus
C_2H_5	C_2H_5	$CH(CH_3)CH_2CH_3$	*****	earthy-caphoraceous
CH_3	n-C_3H_7	$CH_2CH(CH_3)_2$	*****	earthy-caphoraceous
H	n-C_3H_7	$CH_2CH(CH_3)_2$	****	fruity
H	iso-C_3H_7	$CH_2CH(CH_3)_2$	****	fruity-camphor-eucalyptus
H	iso-C_3H_7	$CH(CH_3)CH_2CH_3$	****	earthy
H	$CH_2CH(CH_3)_2$	$CH_2CH(CH_3)_2$	****	linalcol-geraniol
C_2H_5	iso-C_3H_7	iso-C_3H_7	****	eucalyptus-camphor
CH_3	$CH_2CH(CH_3)_2$	$CH(CH_3)CH_2CH_3$	****	earthy-fruity-camphoraceous
iso-C_3H_7	iso-C_3H_7	iso-C_3H_7	****	eucalyptus-geranium
C_2H_5	iso-C_3H_7	$CH(CH_3)CH_2CH_3$	****	earthy-camphoraceous
n-C_3H_7	n-C_3H_7	n-C_3H_7	****	woody
CH_3	n-C_3H_7	$CH_2C(CH_3)_3$	****	earthy-camphoraceous
H	n-C_3H_7	$CH(CH_3)CH_2CH_3$	***	fruity-camphoraceous
H	iso-C_3H_7	$CH_2CH_2CH_2CH_3$	***	fruity
CH_3	n-C_3H_7	$C(CH_3)_3$	***	camphor-eucalyptus
CH_3	n-C_3H_7	$CH_2CH_2CH(CH_3)_2$	***	fruity-earthy
CH_3	$CH(CH_3)CH_2CH_3$	$C(CH_3)_2CH_2CH_3$	***	caramel-fruity-camphoraceous
CH_3	n-C_3H_7	n-C_3H_7	**	earthy-woody-fruity
CH_3	C_2H_5	$C(CH_3)_3$	**	caphor-eucalyptus
CH_3	n-C_3H_7	iso-C_3H_7	**	caphor-eucalyptus
H	C_2H_5	$CH(CH_3)CH_2CH_2CH_3$	**	flowery-fruity
H	n-C_3H_7	$C(CH_3)_3$	**	pineapple-camphoraceous
H	n-C_3H_7	$CH_2CH_2CH(CH_3)_2$	**	fruity (pineapple)
CH_3	n-C_3H_7	$CH_2CH_2CH_2CH_2CH_3$	*	fruity
CH_3	C_2H_5	$CH_2CH_2CH_2CH_3$	*	fruity
H	C_2H_5	$CH_2CH_2CH(CH_3)_2$	*	fruity (pineapple)

Where the compounds used according to the invention have an asymmetric carbon atom either optical isomer may be used in pure form but generally a mixture of optical isomers will be used. In some cases the degree of cooling produced by the compounds will differ as between optical isomers, in which case one or other isomer may be preferred.

The compounds of this invention find utility in a wide variety of compositions for consumption by or application to the human body. Broadly speaking, these compositions

can be divided into comestible and topical compositions, both terms being taken in their broadest possible sense. Thus comestible is to be taken as including not only foodstuffs and beverages taken into the mouth and swallowed, but also other orally ingested compositions taken for reasons other than their nutritional value, e.g. indigestion tablets, antacid preparations, and laxatives. Comestible compositions are also to be taken to include edible compositions taken by mouth, but not necessarily swallowed, e.g. chewing gum. Topical compositions are to be taken as including not only compositions such as perfumes, powders and other toiletries, lotions, liniments, oils and ointments applied to the external surfaces of the human body, whether for medical or other reasons, but also compositions applied to, or which, in normal usage, come in contact with, internal mucous membranes of the body, such as those of the nose, mouth, or throat, whether by direct or indirect application or inhalation, and thus include nasal and throat sprays, dentifrice, mouthwash and gargle compositions. Also included within the present invention are toilet articles such as cleansing tissues and tooth-picks impregnated or coated with the active cooling compound.

A further class of compositions included within the scope of this invention are tobacco and associated articles e.g. pipe and cigarette filters, especially filter tips for cigarettes.

The compositions of this invention will contain an amount of the active cooling compound sufficient to stimulate the cold receptors in the areas of the skin or mucous membrane with which the compositions come into contact and thereby promote the desired cold sensation. As the degrees and longevity of cooling sensation varies from compound to compound the quantity of stimulant used in each composition will vary widely. As a guide, it may be said that, with the more active compounds, a significant cooling sensation is achieved upon application to the skin of as little as 0.05 ml of a 1% solution of the active ingredient in ethanol. For the less active compounds a significant cooling effect is achieved only with more concentrated solutions, e.g. 5% by weight or more of the active ingredient. It must also be admitted that such skin tests are somewhat subjective, some individuals experiencing a greater or lesser cooling sensation than others when subjected to the same test.

In formulating the compositions of this invention the active cooling compound will usually be incorporated into a carrier which may be completely inert or which may be or contain other active ingredients. A wide variety of carriers will be suitable, depending upon the end use of the composition, such carriers including solids, liquids, emulsions, foams and gels. Typical carriers for the active cooling compound include aqueous or alcoholic solutions; oils and fats such as hydrocarbon oils, fatty acid esters, long chain alcohols and silicone oils; finely divided solids such as starch or talc; cellulosic materials such as paper tissue; tobacco; low-boiling hydrocarbons and halohydrocarbons used as aerosol propellants; gums and natural or synthetic resins.

In most compositions according to the invention the carrier will be or contain as an adjuvant one or more of the following: an antacid, antiseptic or analgesic, a flavourant, colourant, or odourant, or a surfactant.

The following illustrate the range of compositions into which the active cooling compounds can be incorporated:

1. Edible or potable compositions including alcoholic and non-alcoholic beverages, confectionery, chewing gum; cachous; ice cream; jellies;

2. Toiletries including after shave lotions, shaving soaps, creams and foams, toilet water, deodorants and antiperspirants, "solid colognes", toilet soaps, bath oils and salts, shampoos, hair oils, talcum powders, face creams, hand creams, sunburn lotions, cleansing tissues, dentifrices, toothpicks, mouthwashes, hair tonics, eyedrops;

3. Medicaments including antiseptic ointments, pile ointments, liniments, lotions, decongestants, counter-irritants, cough mixtures, throat lozenges, antacid and indigestion preparations, oral analgesics;

4. Tobacco preparations including cigars, cigarettes, pipe tobacco, chewing tobacco and snuff; tobacco filters, especially filter tips for cigarettes;

5. Miscellaneous compositions such as water soluble adhesive compositions for envelopes, postage stamps, and adhesive labels.

Particular preparations according to the invention are discussed in more detail below.

Edible and Potable Compositions.

The edible and potable compositions of this invention will contain the active cooling compound in combination with an edible carrier and usually a flavouring or colouring agent. The particular effect of the cooling compounds is to create a cool or fresh sensation in the mouth, and in some cases, even in the stomach, and therefore the compounds find particular utility in sugar-based confactionery such as chocolate, boiled sweets and candy, in ice cream and jellies and in chewing gum. The formulation of such confections will be by ordinary techniques and according to conventional recipes and as such forms no part of this invention. The active compound will be added to the recipe at a convenient point and in amount sufficient to produce the desired cooling effect in the final product. As already indicated, the amount will vary depending upon the particular compound, the degree of cooling effect desired and the

strength of other flavourants in the recipe. For general guidance, however, amounts in the range 0.1 to 5.0% by weight based on the total composition will be found suitable.

Similar considerations apply to the formulation of beverages. Generally speaking the compounds will find most utility in soft drinks e.g. fruit squashes, lemonade and cola, but may also be used in alcoholic beverages. The amount of compound used will generally be in the range 0.05 to 2.5% by weight based on the total composition.

Toiletries.

Because of the cooling sensation imparted to the skin, a major utility of the cooling compounds will be in a wide range of toilet preparations and toilet articles. The particular preparations discussed below are to be taken as exemplary.

A major utility will be in after shave lotions and toilet water, where the compound will be used in alcoholic or aqueous alcoholic solution, such solutions usually also containing a perfume or mild antiseptic or both. The amount of compound added to the formulation will usually be in the range 0.1 to 10% by weight based on the total composition.

Another field of utility will be soaps, shampoos and bath oils where the compound will be used in combination with an oil or fat or a natural or synthetic surfactant e.g. a fatty acid salt or a lauroyl-sulphate salt, the composition usually also containing an essential oil or perfume. The range of soap compositions will include soaps of all kinds e.g. toilet soaps, shaving soaps and shaving foams. Usually the compound will be added to the formulation in amount of from 1.0 to 10% by weight.

A further class of toilet compositions into which the compounds may be incorporated includes cosmetic creams and emollients, such creams and emollients usually comprising a base emulsion and optionally a range of ingredients such as wax, preservative, perfume, antiseptics, astringents, and pigments. Also included within this class are lipstick compositions such compositions usually comprising an oil and wax base into which the compound can be incorporated along with the conventional ingredients i.e. pigments and perfumes. Once again the formulation of such compositions, apart from the incorporation of the cooling compound, usually in an amount of from 0.05 to 10.0% by weight, is conventional.

Compositions for oral hygiene containing the cooling compounds include mouthwash, gargle and dentifrice compositions. The first two may be considered together and will usually comprise an aqueous, alcoholic, or aqueous-alcoholic solution of an antiseptic often coloured or flavoured for palatability, to which the coolant is added to an amount of from 0.01 to 5% by weight.

Dentifrice compositions may be of the solid block, powder, paste or liquid type and will usually comprise a finely divided abrasive or polishing material, e.g. precipitated chalk, silica, magnesium silicate, aluminium hydroxide or other similar materials well known in the art, and a detergent or foaming agent. Optional ingredients which may also be included are flavouring agents and colourants, antiseptics, lubricants, thickeners, emulsifiers or plasticizers. The amount of coolant added in such compositions will generally be from 0.1 to 5.0% by weight based on the total composition.

Medicaments.

Because of their cooling effect on the skin and on the mucous membranes of the mouth, throat and nose and of the gastrointestinal tract the cooling compounds may be used in a variety of oral medicines, nasal and throat sprays, and topical compositions, particularly where a counter-irritant is required. In particular the coolants may be formulated into antacid and indigestion remedies, in particular those based on sodium bicarbonate, magnesium oxide, calcium or magnesium carbonate, aluminium or magnesium hydroxide or magnesium trisilicate. In such compositions the coolant will usually be added in an amount of from 0.01 to 2.0% by weight.

The coolants may also be included in oral analgesic compositions e.g. with acetylsalicylic acid or its salts.

Because of their volatility and their effect on the mucous membranes of the nose and bronchial tract, the compounds used in the present invention are particularly useful in nasal decongestants e.g. in combination with ephedrine, and in throat lozenges and pastilles, and also in olfactory ointments and liniments used as vapour rubs and containing an oleaginous base into which the coolant may be incorporated in amounts of from 1.0 to 10% by weight.

Tobacco Preparations.

The coolants of this invention may be incorporated directly into tobacco to give a cool effect when smoking but without the attendant strong and characteristic odour which is associated with mentholated tobacco and cigarettes. However, a more advantageous utilisation of the coolants of this invention is in pipe or cigarette filters, in particular, filter tipped cigarettes. The pad of filter material, which may be of any of the well known types, e.g. cellulose acetate, paper, cotton α-cellulose or asbestos fiber, is simply impregnated with an alcoholic solution of the coolant and dried to deposit the coolant in the filter pad. The effect is to give a pleasant cool sensation in the mouth when the cigarette is

smoked. As little as 0.1 mg [redacted]e coolant is effective.

Compositions of this invention are illustrated by the following Examples.

EXAMPLE I

After Shave Lotion

An after shave lotion was prepared according to the following recipe by dissolution of the ingredients in the liquid and cooling and filtering:—

Denatured Ethanol	75%
Diethyl Phthalate	1.0%
Propylene Glycol	1.0%
Lactic Acid	1.0%
Perfume	3.0%
Water	to 100%

Into the base lotion was added 3% by weight based on the total composition of 3 - ethyl - 4 - methyl - 3 - hexanol.

When the final lotion is applied to the face a clearly noticeable cooling effect becomes apparent after a short interval of time.

EXAMPLE II

Eye Lotion

An eye lotion was prepared containing the following ingredients:—

Witch Hazel	12.95%
Boric Acid	2.00%
Sodium Borate	0.50%
Allantoin	0.05%
Salicylic Acid	0.025%
Chlorobutol	0.02%
Zinc Sulphate	0.004%
Water	to 100%

To the formulation was added 0.01%, based on the total composition of 2 - methyl - 3 - isopropyl - 3 - hexanol. When used to bathe the eyes a cool fresh sensation is apparent on the eyeball and eyelids.

EXAMPLE III

Toothpaste

The following ingredients were mixed in a blender:—

Dicalcium Phosphate Dihydrate	40%
Sodium Lauryl Sarcosinate	1.5%
Glycerol	30%
Sodium Carboxymethyl Cellulose	1.5%
Saccharin Sodium	0.2%
Sodium Benzoate	0.2%
Water	26.6%

Shortly before completion of the blending operation 1.5% by weight of 4 - isopropyl - 4 - heptanol was added to the blender.

When applied as a toothpaste, a cooling effect is noticed in the mouth.

EXAMPLE IV

Soft Sweet

Water was added to icing sugar at 40°C to form a stiff paste. 1% of 4 - *n* - propyl - 4 - heptanol was then stirred into the paste and the mixture allowed to set. A soft sweet mass resulted having the characteristic cooling effect in the mouth of peppermint but without the minty flavour or odour.

EXAMPLE V

Cigarette Tobacco

A proprietary brand of cigarette tobacco was impregnated with 2,4 - dimethyl - 3 - ethyl - 3 - pentanol and was rolled into cigarettes each containing approximately 0.001 gm of active compound. Smoking the impregnated cigarettes produced a cool effect in the mouth characteristic of mentholated cigarettes.

A similar effect is noticed when smoking a proprietary brand of tipped cigarette, the coolant being used to impregnate the filter tip rather than the tobacco.

EXAMPLE VI

Antiseptic Ointment

An ointment was prepared according to the following formulation:—

Cetyltrimethylammonium bromide	4.0%
Cetyl Alcohol	6.0%
Stearyl Alcohol	6.0%
White Paraffin	14.0%
Mineral Oil	21.0%
Water	to 100%

The ingredients were mixed, warmed to 60°C and emulsified in a high-speed blender. Added to the mixture during blending was 4% of 2,4 - dimethyl - 4 - heptanol.

The final ointment when applied to the skin gave rise to a marked cooling effect.

EXAMPLE VII

Aerosol Shaving Soap

An aerosol shaving soap composition was formulated according to the following recipe:—

Stearic Acid	6.3%
Lauric Acid	2.7%
Triethanolamine	4.6%
Sodium Carboxymethyl Cellulose	0.1%
Sorbitol	5.0%
Water	to 100%
Flavourant	0.5%

The composition was prepared by fusing the acids in water, adding the triethanolamine, cooling and adding the other constituents. To the mixture was then added 2% of 2 - methyl - 4 - heptanol. The composition was then packaged in an aerosol dispenser under pressure of a butane propellant.

When used having a fresh cool sensation was distinctly noticeable on the face.

EXAMPLE VIII

Toilet Water

A toilet water was prepared according to the following recipe:—

Denatured ethanol	75.0%
Perfume	5.0%
Water	to 100%

To the recipe was added 4.0%, based on the total composition, of 2,5 - dimethyl - 3 - hexanol.

As with the after shave lotion, a cooling effect was clearly noticeable on the skin well after the termination of any cooling effect attributable to the evaporation of the alcoholic carrier.

EXAMPLE IX

Deodorant Composition

A deodorant composition suitable for formulation and dispensing as an aerosol under pressure of a suitable propellant was formulated according to the following recipe:—

Denatured ethanol	96.9%
Hexachlorophene	2.0%
Isopropyl myristate	1.0%
Perfume	0.1%

To the composition was added 4% by weight of 2,6 - dimethyl - 4 - heptanol. Application of the final composition gave rise to a definite cooling sensation on the skin.

EXAMPLE X

Hair Shampoo

Sodium lauryl ether sulphate, 10 g, was dispersed in 90 g water in a high speed mill. To the dispersion was added 4.5% by weight of 2,4 - dimethyl - 4 - heptanol. When the hair is washed using the shampoo a fresh, cool sensation is noticed on the scalp.

EXAMPLE XI

Solid Cologne

A clid cologne was formulated according to the following recipe:—

Denatured ethanol	74.5%
Propylene Glycol	3.0%
Sodium Stearate	5.0%
Perfume	5.0%
Water	to 100%

The sodium stearate was dissolved by stirring in a warm mixture of the ethanol, propylene glycol and water. To the solution was added the perfume and 4.0% of 2,4 - dimethyl - 3 - isopropyl - 3 - pentanol and the mixture then allowed to solidify into a waxy cake.

When applied to the forehead a distinct cooling effect is noticeable.

EXAMPLE XII

Mouthwash

A concentrated mouthwash composition was prepared according to the following recipe:—

Ethanol	3.0%
Borax	2.0%
Sodium Bicarbonate	1.0%
Glycerol	10.0%
Flavourant	0.4%
Thymol	0.03%
Water	to 100%

To the composition was added 0.2% of 2,4 - dimethyl - 3 - ethyl - 3 - pentanol.

When diluted with approximately 10 times its own volume of water and used to rinse the mouth a cooling effect is obtained in the mouth.

EXAMPLE XIII

Soft Drink

A soft drink concentrate was prepared from the following recipe:—

Pure orange juice	60%
Sucrose	10%
Saccharin	0.2%
Orange flavouring	0.1%
Citric acid	0.2%
Sulphur dioxide	trace amount
Water	to 100%

To the concentrate was added 0.1% of 4 - isopropyl - 4 - heptanol.

The concentrate was diluted with water and tasted. An orange flavour having a pleasantly cool after-effect was obtained.

EXAMPLE XIV

Boiled Sweet

99.5% sucrose and 0.5% citric acid were carefully fused together in the presence of a trace of water. Just before casting the melt onto a chilled plate 0.5% of 3,3,4,5 - tetramethyl - 4 - heptanol was rapidly stirred in. The melt was then cast. A boiled sweet resulted having a marked cooling effect on the mouth.

EXAMPLE XV

Indigestion Tablet

The following ingredients were ground together:—

Magnesium carbonate	49.5%
Sorbitol	49.4%
Saccharin	0.1%
Talc	1.0%

Added to the mixture during grinding was 0.1% of 4 - *n* - propyl - 4 - heptanol. After

mixing the mixture was p[illegible] into 0.5 g tablets.

Taken by mouth and swallowed the tablets produced, after a short interval of time, a noticeable cooling effect in the stomach.

EXAMPLE XVI

Cleansing Tissue

A cleansing liquid was prepared having the formulation:—

Triethanolamine Lauryl Sulphate	1.0%
Glycerol	2.0%
Perfume	0.95%
Water	to 100%

To this liquid was added 4% of 4 - isopropyl - 4 - heptanol. A paper tissue was then soaked in the liquid.

When the impregnated tissue was used to wipe the skin a fresh cool sensation developed on the skin after a short interval.

EXAMPLE XVII

Hydrophilic Ointment

A hydrophilic ointment was prepared having the following formulation:—

Propylene Glycol	12%
1 - Octadecanol	25%
White Soft Paraffin	25%
Sodium Lauryl Sulphate	1%
Water	to 100%

The sodium lauryl sulphate was added to the water and heated to 60°C. The paraffin was melted by heating to 60°C and was then added to the sodium lauryl sulphate mixture with stirring. Propylene glycol and 1 - octadecanol were then added to this mixture.

To the resultant mixture was added 3% of 3 - ethyl - 4 - methyl - 3 - hexanol. The final ointment when applied to the skin gave rise to a marked cooling effect.

EXAMPLE XVIII

Vapour Rub

4% of 2,4 - dimethyl - 3 - ethyl - 3 - pentanol was mixed into 96% of white soft paraffin.

When rubbed onto the skin a pleasant cooling vapour is released.

EXAMPLE XIX

Liniment

A liniment was prepared according to the following formulation:—

Methyl Salicylate	25%
Eucalyptus Oil	10%
Arachis Oil	to 100%

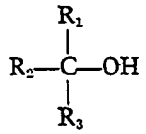
To the composition was added 4% of 2 - methyl - 3 - isopropyl - 3 - hexanol.

When the final composition[illegible] applied to the skin a clearly noticeable cooling effect became apparent after a short interval of time.

The above Examples illustrate the range of compounds and the range of compositions included in the invention. However, they are not to be taken as limiting the scope of the invention in any way. Other compounds within the general formula will be equally suitable for use in the compositions of Examples I—XIX and the physiological effect obtained with the compounds of the invention will recommend their use in a wide variety of other compositions where the cooling effect will be of value.

WHAT WE CLAIM IS:—

1. A manufactured product for application to or consumption by the human body comprising a physiologically active ingredient capable of stimulating the cold receptors of the nervous system of the body and a carrier therefore, said carrier constituting or providing a vehicle by means of which said ingredient may be brought into contact with the skin or other surface tissue of the body upon use of the said product, said carrier comprising a manufactured article or preparation into which the said ingredient is incorporated by admixture or impregnation and being other than a liquid or mixture of liquids which serve as solvent for the said ingredient and which contain no other ingredient, wherein said physiological, active ingredient is a secondary or tertiary alkanol of the formula:



where R_1 is H or C_1—C_5 alkyl; R_2 is C_2—C_5 alkyl; R_3 is C_2—C_5 alkyl; with the provisos that, i) when R_1 is H, at least one of R_2 and R_3 is a branched chain group; ii) when R_1 is methyl and one of R_2 and R_3 is isobutyl, the other is selected from ethyl, *n* - propyl, isopropyl, *n* - butyl, sec.butyl, tert.butyl and straight and branched chain amyl; and iii) R_1, R_2 and R_3 together provide a total of from 7—10 carbon atoms.

2. A product according to claim 1, wherein said ingredient is of the formula defined where R_1 is H, R_2 and R_3 together provide a total of from 7—9 carbon atoms and at least one of R_2 and R_3 has branching in an alpha or beta position relative to the C atom shown in the formula.

3. A product according to claim 1 or 2, wherein said ingredient is of the formula defined, where R_1 is methyl, ethyl or propyl, and R_1, R_2 and R_3 together provide a total of from 8—10 carbon atoms.

4. A product according to any one of claims 1—3, wherein said carrier is an edible preparation containing an edible base material and a flavourant or colourant.

5. A product of matter according to claim 4, wherein said carrier is a chewing gum.

6. A product according to any one of claims 1—3, wherein said carrier is an orally or topically administrable pharmaceutical preparation, comprising an orally or topically acceptable carrier and an orally or topically administrable pharmaceutically active ingredient.

7. A product according to any one of claims 1—3, wherein said carrier is a beverage containing a potable base material and a flavourant or colourant.

8. A product according to any one of claims 1—3, wherein said carrier is a dentifrice.

9. A product according to any one of claims 1—3, wherein said carrier is a mouthwash comprising an aqueous or aqueous/alcoholic solution of an orally acceptable antiseptic.

10. A product according to any one of claims 1—3, wherein said carrier is a lotion for topical application to the body which comprises an aqueous or aqueous/alcoholic base and one or more of the following, a colourant, an odourant or an antiseptic.

11. A product according to any one of claims 1—3, wherein said carrier is an ointment, cream, or oil for topical application to the body.

12. A product according to any one of claims 1—3, wherein said carrier is a toilet soap or shampoo.

13. A product according to any one of claims 1—3, wherein said carrier is a shaving soap or foam.

14. A product according to any one of claims 1—3, wherein said carrier is a liquid impregnated cleansing tissue.

15. A product according to any one of claims 1—3, wherein said carrier is or contains tobacco.

16. A product according to claim 15, wherein said carrier is a cigarette.

17. A product according to claim 16, wherein said carrier is a filter-tipped cigarette and wherein said ingredient is impregnated in the filter tip.

18. A product according to claim 1, being a product substantially as hereinbefore described in any one of the foregoing Examples.

19. A method of stimulating the cold receptors of the nervous system of the body, other than as part of a medical treatment, which comprises applying to the skin, or other surface tissue of the body, a compound of the formula defined in claim 1 or as modified by claim 2 or 3.

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